Published in final edited form as:

Int J Drug Policy. 2019 July ; 69: 1–7. doi:10.1016/j.drugpo.2019.02.009.

Evaluation of contingency management as a strategy to improve HCV linkage to care and treatment in persons attending needle and syringe programs: A pilot study

B.L. Norton^{a,*}, M.A. Bachhuber^a, R. Singh^b, L. Agyemang^a, J.H. Arnsten^a, C.O. Cunningham^a, A.H. Litwin^{a,**}

^aDivision of General Internal Medicine, Montefiore Medical Center, United States

^bNew York University, United States

Abstract

Background: A greater proportion of HCV-infected people who inject drugs (PWID) need to be linked to care for HCV antiviral treatment. This study sets out to evaluate the efficacy of contingency management (CM) for improving HCV linkage to care, treatment initiation, adherence, and cure for PWID recruited from a needle and syringe program.

Methods: Between March 2015 and April 2016, 20 participants were enrolled into the CM arm, and then subsequently enrolled 20 participants in the enhanced standard of care (eSOC) arm. Participants in the eSOC arm received an expedited appointment and a round-trip transit card. Participants enrolled in the CM arm received eSOC plus \$25 for up to ten HCV clinical visits and \$10 for each returned weekly medication blister pack. Adherence was measured via electronic blister packs.

Results: Overall the median age was 47 years; most were men (67%) and Hispanic (69%). There were no significant differences in demographic characteristics between participants in the study arms. In the CM arm 74% were linked to HCV care, compared to 30% in the eSOC arm ($p = 0.01$). In the CM arm, 75% (9/12) of treatment eligible participants initiated treatment, compared to 100% (4/4) in the eSOC arm ($p = 0.53$). All patients (9/9) achieved cure in the CM arm, as compared to 75% (3/4) of patients in the eSOC arm. There were no differences in adherence between study arms.

Conclusions: In this pilot study, contingency management led to higher rates of HCV linkage to care for PWID, as compared to standard of care. CM should be considered as a possible intervention to improve the HCV treatment cascade for PWID.

*Corresponding author at: DO, MPH Division of General Internal Medicine and Infectious Diseases Montefiore Medical Center, Albert Einstein College of Medicine, 3300 Kossuth Avenue Bronx, NY, 10454, United States. bnorton@montefiore.org (B.L. Norton).

**Corresponding author at: MPH Department of Medicine Greenville Health System, 701 Grove Road Greenville, SC, 29615, United States. alitwin@ghs.org (A.H. Litwin).

Conflict of interest statement

Brianna Norton, Marcus Bachhuber, Reena Singh, Linda Agyemang, and Julia Arnsten have no conflicts of interest.

Keywords

Persons who inject drugs (PWID); HCV; Linkage to care; Contingency management; Syringe exchange programs

Introduction

The majority of new and chronic Hepatitis C virus (HCV) infections that occur in high income countries are among people who inject drugs (PWID) (Degenhardt et al., 2017; Hajarizadeh, Grebely, & Dore, 2013). Currently there are 6.1 million PWID infected with HCV worldwide, and the mortality from HCV continues to rise (Grebely, Larney et al., 2019; Hajarizadeh et al., 2013; Stanaway et al., 2016). New oral direct acting antiviral (DAA) treatment regimens offer cure rates over 95% in as little as 8 weeks, have few side effects (Recommendations for testing, managing, & treating hepatitis C, 2017), and are associated with decreased mortality (Backus et al., 2011; Dieperink et al., 2014; van der Meer et al., 2012) and viral transmission (Grebely, Matthews, Lloyd, & Dore, 2013; Hellard et al., 2015; Martin et al., 2013, 2016).

Although people who inject drugs (PWID) represent the over-whelming majority of HCV infections in high income countries and are a priority population to achieve HCV elimination worldwide, linkage of PWID to HCV care and treatment has been poor (Bruggmann & Grebely, 2015; Day et al., 2018; Martin et al., 2013). In the United States (US), fewer than 33% of PWID with HCV infection have undergone HCV evaluation and fewer than 10% have initiated HCV treatment (Alavi et al., 2014; Grebely et al., 2007; Hellard, Sacks-Davis, & Gold, 2009; Iversen et al., 2017; Mehta et al., 2008; Midgard, Bramness, Skurtveit, Haukeland, & Dalgard, 2016; Treloar, Newland, Rance, & Hopwood, 2010; Treloar, Hull, Dore, & Grebely, 2012).

Despite DAAs being available in New York State and covered by State insurance, only 14% of HCV infected persons living in New York City have been cured (NYC Department of Health & Mental Hygiene, 2017). Due to multiple barriers, PWID do not often access traditional health care settings. As such, needle and syringe programs (NSPs) are a promising setting to identify PWID with HCV infection and link them to HCV care (Grebely et al., 2017; Iversen et al., 2017). In 2013, 204 NSPs distributed 46 million syringes and provided harm reduction and preventive medical services to 1.5 million PWID throughout the US (Centers for Disease & Prevention, 2010; Des Jarlais, Nugent, & Solberg, 2014; Des Jarlais et al., 2015). Though NSPs provide HCV screening and identify high rates of HCV infection (range 31%–68%) (Eckhardt et al., 2017; Hochstatter et al., 2017; Salek et al., 2017), linkage to HCV care remains uncommon and NSP-based interventions that effectively promote linkage to HCV care are urgently needed (Hochstatter, Westergaard, Hess, Hull, & Peng, 2016; Joseph, Kofman, Larney, & Fitzgerald, 2013).

Contingency management (CM), the use of financial incentives, has been utilized to improve linkage to care among vulnerable populations (El-Sadr et al., 2017; Metsch et al., 2016; Solomon et al., 2014). CM relies on the behavioral economic theory that patients often delay healthy choices because of uncertainty in long-term gains (i.e., treating a disease that takes

years to damage the liver and produce symptoms) and instead make unhealthy choices (e.g., disengagement in HCV care) for more immediate economic gains (e.g., saving time, transportation costs, and the cost of copayments) (Giles, Robalino, McColl, Sniehotta, & Adams, 2014; Lagarde, Haines, & Palmer, 2007; Operario, Kuo, Sosa-Rubi, & Galarraga, 2013). CM has the potential to increase linkage to HCV care among PWID by providing an immediate gain in financial resources tied to engagement in HCV care. In previous studies, CM was both acceptable to and effective in linking people with HIV infection who use drugs to HIV care (Bassett, Wilson, Taaffe, & Freedberg, 2015), but whether CM is effective for linking people to HCV care is unknown.

The goal of this prospective pilot study was to assess the effectiveness of contingency management (CM) compared to an enhanced standard of care (eSOC) for promoting linkage to care (attending a healthcare visit for HCV evaluation), treatment initiation, adherence, and SVR for HCV-infected individuals attending an NSP. Rates of linkage to care (attendance at a baseline HCV visit at a nearby health center) was hypothesized to be higher in the CM versus the control arm. Rates of treatment initiation, completion, and SVR were compared between arms; and adherence was examined over time among all subjects who initiated DAA treatment.

Methods

Recruitment setting

From March 2015 to April 2016, PWID with HCV infection were recruited from New York Harm Reduction Educators (NYHRE), an NSP in New York City. NYHRE is the largest harm reduction agency in New York City with over 35 staff members and 4000 annual clients, of whom each have a unique ID number and card that allows them to carry syringes. From one community-based drop-in center and nine street-side van locations, NYHRE provides syringe exchange and mental health counseling, referrals for medical, dental, psychiatric and substance use disorder treatment, and other supportive services. The majority of NYHRE's clients are Hispanic or Black, male, 40–49 years old, and PWID. NYHRE's diverse staff members have received HCV education and training on HCV screening and DAA treatment options.

Participant recruitment and eligibility criteria

As part of an ongoing HCV testing program, NYHRE staff offer rapid HCV antibody tests to all clients. Flyers were placed in the drop-in center advertising the study. During the study period, research staff approached clients for potential study enrollment that were identified by NYHRE staff as having an HCV + antibody. For clients who expressed interest in participating, research staff obtained written informed consent and collected contact and demographic information. Study inclusion criteria were: 1) client of NYHRE, 2) HCV antibody positivity, 3) at least 18 years of age, 4) fluency in English, and 5) medical insurance accepted by the treatment health center.

Treatment setting and protocol for all participants

All participants, regardless of arm, received HCV evaluation and treatment at the Comprehensive Health Care Center, a Federally Qualified Health Center affiliated with Montefiore Medical Center in the Bronx, New York. This health center is located five miles from NYHRE and is accessible by public transportation. All HCV treatment is delivered by a physician trained in HCV care and experienced in the treatment of substance use disorder. Interferon-free DAA treatment was offered at this clinic since November 2014, 4 months prior to study enrollment. HCV care is also supported by an HCV care coordinator who assists patients with scheduling appointments, makes reminder calls, and obtains prior authorizations for DAAs and other HCV medications. Most patients treated for HCV at this health center have Medicaid (state government health insurance). In New York State individuals qualify for Medicaid if their income is 138% the federal poverty level (one-person yearly salary of \$12,140 USD). In New York State, Medicaid does not restrict HCV medication access based on either fibrosis level nor drug use (Barua et al., 2015).

The HCV treatment protocol at the health center included 9–10 visits depending on the length of treatment regimen (Table 1): baseline HCV evaluation, review of laboratory results, HCV treatment initiation, HCV treatment week 2 (per protocol at this primary care clinic), HCV treatment week 4, HCV treatment week 8, HCV treatment week 12, HCV treatment week 24 for those with genotype 3, 4 weeks post HCV treatment completion (SVR4), and 12 weeks post HCV treatment completion (SVR12). The baseline evaluation visit consisted of a full clinical and laboratory HCV evaluation, including noninvasive assessment of liver fibrosis stage which was obtained by using the FibroSure® blood test, and referral for abdominal ultrasound if there was evidence of cirrhosis. Participants were ineligible for HCV treatment as determined by the HCV physician if they had impaired renal function (defined as creatinine clearance < 30 mL/min as calculated by the Cockcroft-Gault equation), decompensated liver disease, or an estimated survival of less than one year.

All participants received DAA treatment as per the American Association for the Study of Liver Diseases/Infectious Diseases Society of America (AASLD/IDSA) guidelines (Recommendations for testing, managing, & treating hepatitis C, 2017). Study participants who initiated HCV treatment received DAAs packaged in weekly electronic blister packs. Participants received two weeks of blister packs at the HCV treatment initiation visit, two weeks of packs at HCV treatment week 2, four weeks of packs at HCV treatment week 4, and then every 4 weeks until treatment completion. In addition, urine toxicology screening was ordered and encouraged at each visit to facilitate an ongoing discussion about harm reduction. All HCV clinical care (i.e., visits, laboratory tests) was billed to participants' health insurance. DAA medication was also obtained through the participants medical insurance. In past studies with NSP clients, insurance coverage was high: 83% Medicaid/Medicare, 5% other insurance, and 12% were uninsured (Fox, Chamberlain, Frost, & Cunningham, 2015). If participants are uninsured, NSP case managers assist the participant in obtaining Medicaid, which is then available for use by the following month.

Study conditions

Enhanced standard of care (eSOC)—A comparator arm was developed for this study because the protocol for linking PWID to HCV care was heterogeneous and poorly defined at the NSP. The eSOC arm consisted of an expedited appointment at the health center (within one week of study enrollment) and a round-trip transit fare card. In addition, the HCV care coordinator made a reminder call to each study participant one day prior to the baseline HCV evaluation visit. If participants missed the baseline appointment, study staff would make two additional attempts to reschedule participants, as was also done in the CM arm.

CM intervention—The CM intervention arm consisted of enhanced standard of care (eSOC, described above) plus financial incentives (all in US dollars) for attendance at HCV visits, return of medication blister packs, and successful early clinical outcome while on HCV treatment (undetectable HCV viral load at treatment week 4). Participants received \$25 for attending each of the 9 HCV treatment visits and \$10 for each weekly blister pack that was returned, regardless of level of adherence. Participants also received \$50 for an undetectable HCV viral load at HCV treatment week 4 as an incentive for adherence. This decision regarding adherence was based on the fact that 100% [213/213] of subjects assigned to sofosbuvir/ledipasvir for 12 weeks in the ION-1 trial had an undetectable HCV viral load at week 4 (Afdhal et al., 2014). For attending all visits, depositing all blister packs, and achieving an undetectable viral load at week 4, participants could receive up to a total maximum of \$395 for a 12-week regimen, or \$540 for a 24-week regimen.

Allocation to study arms—Using convenience sampling in this pilot study, we enrolled a total of 40 participants in this study based on the limitations in funding for the contingency management arm. Between March and September 2015, 20 participants were enrolled into the CM arm. There was a 3-month washout period between enrolling the last participant into the CM arm and enrolling the first participant into the eSOC arm, so that there was sufficient time between interventions such that the eSOC arm were unaware or less aware of potentially “missing out” on the CM arm. Between December 2015 and April 2016, 20 participants were then enrolled into the eSOC arm. Randomization was felt to be too difficult in this trial due to the concern that those randomized to eSOC (referral) would feel that they were “missing out” on the CM (financial incentives), particularly since many participants are living in poverty. As such, we chose to enroll sequentially, and with a wash-out period between arms.

Primary and secondary outcomes—Our primary outcome was linkage to HCV care, defined as attending the baseline HCV evaluation visit within 3 months of study enrollment. Secondary outcomes included HCV treatment initiation, HCV medication adherence, and HCV cure (SVR12). HCV treatment initiation was defined as receiving a prescription for at least one DAA within 1 year of the baseline evaluation visit. HCV medication adherence was defined as the percentage of treatment days during which the participant took a dose of the prescribed DAA, measured using electronic Med-ic® blister packs, which have a 99.6% event accuracy (Information Mediary Corp, 2019). Adherence was measured over 84 days (12 weeks of therapy), and was based on a daily adherence window, meaning that participants received credit if the dose was taken during the specified day. HCV cure was

defined as an undetectable HCV viral load at least 12 weeks post-treatment (SVR12). Participants who did not attend the visit 12 weeks post-treatment were considered to have virologic failure; we allowed a window period of 3 months to attend this visit. Plasma HCV RNA was measured with the COBAS Taqman HCV/HPS v2.0 assay (Roche, Molecular Diagnostics, Pleasanton, California; lower limit of quantification 25 IU/mL; limit of detection 15 IU/mL).

Other participant characteristics—For participants achieving linkage to HCV care, study staff conducted a 22 item in-person interview during the baseline HCV evaluation visit that enquired about housing status (homeless was defined as either street homeless or living in a shelter), HCV risk behaviors (Chawarski, Pakes, & Schottenfeld, 1998), drug use in the past 30 days (Addiction Severity Index) (McLellan et al., 1992), and alcohol use via the AUDIT questionnaire (Saunders, Aasland, Babor, de la Fuente, & Grant, 1993). However, for those participants who were not linked to HCV care, only basic demographic information was collected at the NSP.

Statistical methods—First, frequencies or means for demographic characteristics for all participants were tabulated and then compared between study arms. For participants who achieved linkage to HCV care and were treatment eligible, frequencies or means for other participant characteristics were tabulated and then compared between study arms. All comparisons were performed using chi-square tests for categorical variables and t-tests for continuous variables.

Frequencies of dichotomous outcomes (linkage to HCV care, HCV treatment initiation, and HCV cure) were tabulated and then compared between study arms using fisher exact tests. For linkage to HCV care, the denominator was all enrolled patients. For HCV treatment initiation and HCV cure, the denominator was treatment eligible patients (i.e., the number of patients linked to care minus the number found ineligible for HCV treatment due to a negative HCV RNA). To analyze HCV medication adherence, weekly adherence percentages between study arms were compared using a mixed-effects model that accounted for within-subject outcome correlations. Weekly changes in adherence rates (number pills/seven days) for all participants receiving treatment over the study period were estimated by fitting a mixed-effects linear regression model with weekly adherence percentage as the dependent variable and study week as the main independent variable.

This study was approved by Albert Einstein College of Medicine Institutional Review Board.

Results

Enrollment and demographic characteristics

Between March 2015 and April 2016, 40 participants were enrolled into the study. After excluding one participant due to lack of appropriate health insurance, 19 participants were in the CM arm and 20 in the eSOC arm (Fig. 1). Of the 39 study participants, the median age was 46.5 years (IQR 39-54 years); most were men (67%) and Hispanic (69%). There were no significant differences in demographic characteristics between participants in the two study

arms (Table 2). 6/20 (30%) participants linked to HCV care in the eSOC arm ($p = 0.01$; Fig. 2). Two participants in the CM arm and two participants in the eSOC arm were determined not to have current HCV infection (HCV RNA negative) and were therefore ineligible for HCV treatment. Of the 16 participants who were linked to HCV care and eligible for HCV treatment, most were male (69%), with a median age of 50 (IQR 42, 55), either Hispanic (38%) or Black (44%), and half were homeless (50%) (Table 3). All 16 patients had HCV genotype 1, and over half (58%) had either F3 or F4 fibrosis. Four participants were HIV/HCV coinfection, and 75% presented with detectable HIV viral loads. At baseline, 19% ($n = 3$) of participants reported having a drink that contained alcohol at least 2 times per week. Half of participants (50%, $n = 8$) reported using heroin in the last 30 days, and many reported using cocaine (25%, $n = 4$) or cannabis (38%, $n = 6$). Nearly half (44%, $n = 7$) reported injection drug use in the previous 30 days. All participants who were linked to HCV care and eligible for treatment had urine toxicology tests performed at either the baseline HCV evaluation visit or during HCV treatment; 15/16 (94%) of participants had urine tests positive for illicit drugs. Seven percent (1/15) had cannabis only, 7% (1/15) had cannabis and Phencyclidine (PCP), 13% (2/15) had cocaine only, and 73% (11/15) had both cocaine and opiates in their urine toxicology screen.

HCV treatment initiation, adherence, and HCV cure (Secondary outcomes)

All participants that initiated treatment in both arms were genotype 1 and received sofosbuvir/ledipasvir combination therapy for 12 weeks. In the CM arm, 9/12 (75%) participants initiated treatment, compared to 4/4 (100%) of participants in the eSOC arm ($p = 0.53$). Mean adherence over the 12 weeks of HCV treatment was 74% for the nine participants in the CM arm and 66% for the four participants in the eSOC arm ($p = 0.43$). Mean adherence for all thirteen participants was initially 81% for the first week, then decreased over the 12-week treatment period (-1.4 percentage points per week, 95% CI: $-2.4, -0.3$, $p = 0.01$; Fig. 3). Overall, 9/12 (75%) achieved HCV cure in the CM arm, as compared to 3/4 (75%) in the eSOC arm ($p = 1.0$), Fig. 2. The one patient in the eSOC who did not achieve cure was lost to follow-up and was therefore categorized as a virologic failure; however, this participant did have undetectable HCV virus at their treatment completion visit.

Discussion

In a study among HCV-infected persons at an NSP, participants were more likely to be linked to HCV care when receiving a CM intervention as compared with an expedited referral alone (75% vs. 30%, $p = 0.01$). All subjects that initiated treatment completed therapy and obtained an end of treatment response; and 92% (12/13) achieved SVR. Our findings suggest that CM is a promising intervention to help link PWID in the community to HCV care and treatment. Further, our findings add to existing evidence that HCV cure is readily achievable for PWID.

After HCV antibody testing, the next and most crucial step in the HCV care cascade is linkage into the healthcare system for RNA testing and HCV evaluation. As PWID have high HCV cure rates that are comparable to rates in non-PWID (Dore et al., 2016; Grebely,

Dalgard et al., 2018; Norton et al., 2017), linkage to HCV care could prove to be the major barrier to HCV elimination in the DAA era (Akyar et al., 2016; Hochstatter et al., 2017; Sulkowski, Ward, & Falade-Nwulia, 2017). Based on our and others' findings, many PWID that receive a basic referral to care will not attend an HCV visit (Alavi et al., 2014; Bajis et al., 2017; Fishbein, Lo, Reinus, Gourevitch, & Klein, 2004; Hallinan, Byrne, Agho, & Dore, 2007; Iversen et al., 2017; Mehta et al., 2008); thus, more intensive linkage to care interventions may be needed. CM can aid in both motivation (financial incentive) as well as provide financial resources (transportation costs, copays, food, etc) which may be barriers to accessing care for vulnerable populations. Similar to findings in our study, PWID living with HIV in India who received CM were more likely to be linked into HIV clinical care than control participants (49% vs. 33%, $p < 0.01$) (Solomon et al., 2014). CM appears to be one promising strategy to increase linkage to care for PWID; however larger randomized controlled trials must be conducted in order to definitively answer this question for HCV.

Though this trial was not powered to test more distal cascade of care milestones, CM interventions may also aid in improving the entire HCV cascade of care. In a recent randomized trial to improve HCV treatment initiation (peer mentors vs. CM vs. usual care) among PWID already linked and enrolled within an HIV treatment program, 66% in the usual care arm initiated HCV treatment, as compared with 76% in the CM arm and 88% in the peer mentor arm (Sulkowski et al., 2017). As in our study, PWID had high cure rates (approximately 90%). Another trial examined fixed financial incentives vs. lottery incentives to improve adherence to HCV appointments and medications for participants already linked to care and accepting treatment. SVR rates were high (93% in lottery CM arm vs. 92% in the fixed CM arm), though no different between study arms. CM has also been shown to improve HIV medication adherence and viral suppression; however, these improvements have not been durable after discontinuation of the CM intervention (Rigsby et al., 2000; Rosen et al., 2007; Sorensen et al., 2007). In contrast to HIV, which requires lifelong medication adherence, CM for HCV medication adherence is only needed for a discrete period of time. Our study demonstrated imperfect and modestly declining HCV treatment adherence over time. While this study was not powered to show a difference in adherence rates between study arms, CM may be advantageous for HCV adherence as treatment is rolled out to a larger population of PWID throughout the country and world. Finally, 58% of participants in our study had F3/F4 stage fibrosis, indicating that post cure follow-up for HCC screening may be necessary for many PWID. Intermittent CM (fixed or lottery) could also prove beneficial in keeping these participants engaged in long-term care.

This study has several limitations. While baseline demographic characteristics were similar between the two arms, the participants were not randomized, so unmeasured confounding factors could contribute to our findings. Furthermore, the control arm could have had worsened outcomes if they felt that they had "missed out" on financial incentives; that said there was a 3-month wash-out period such that there was sufficient time between the two arms to minimize the potential bias. Because recruitment of study arms differed in time, secular trends related to DAA availability could not be accounted for, and it is possible that patients treated later on in the trial had more inherent barriers to accessing care. As this was a pilot study to estimate possible effect sizes, it was not fully powered to detect differences in treatment initiation and SVR between arms. This study was unblinded which may have

influenced the behavior of healthcare providers or research staff. Because HCV care data was only collected from the study clinic, all HCV outcomes may not have been captured if participants received care elsewhere. Finally, no model of care will be able to overcome the barriers of medication costs in states or countries that do not cover, or limit treatment coverage based on fibrosis level and drug use.

Conclusions

Although DAAs make HCV cure readily achievable, PWID cannot be treated if they are not linked to care. Given the high prevalence of HCV among PWID, failure to link PWID to care will greatly limit future efforts to eliminate HCV. This study substantiates the need for a larger, adequately powered trial to definitively determine the effect of CM on linkage to care, treatment initiation and SVR for PWID, and provides important power estimates to guide the design of future randomized controlled trials. Contingency management that targets PWID at venues in which they are already receiving services, such as NSPs, is a promising intervention to improve the entire cascade of care for PWID.

Acknowledgments

Funding

This work was supported by the National Institute of Drug Abuse [K23D039060, R01DA034086, K08DA043050, K24DA036955, and R25DA023021]; National Institute of Allergy and Infectious Diseases [5P30AI124414]; and Gilead Sciences [IN-US-334–1415].

Chinazo Cunningham's husband is an employee of Quest Diagnostics, and they own stock and stock options in Quest Diagnostics.

Alain Litwin has received research funding from, and served on advisory boards for, Gilead Sciences and Merck.

References

- Afdhal N, Zeuzem S, Kwo P, Chojkier M, Gitlin N, Puoti M, et al. (2014). Ledipasvir and sofosbuvir for untreated HCV genotype 1 infection. *The New England Journal of Medicine*, 370(20), 1889–1898. 10.1056/NEJMoa1402454. [PubMed: 24725239]
- Akyar E, Seneca KH, Akyar S, Schofield N, Schwartz MP, & Nahass RG (2016). Linkage to Care for Suburban Heroin Users with Hepatitis C Virus Infection, New Jersey, USA. *Emerging Infectious Diseases*, 22(5), 907–909. 10.3201/eid2205.151980. [PubMed: 27089172]
- Alavi M, Raffa JD, Deans GD, Lai C, Krajden M, Dore GJ, et al. (2014). Continued low uptake of treatment for hepatitis C virus infection in a large community-based cohort of inner city residents. *Liver International : Official Journal of the International Association for the Study of the Liver*, 34(8), 1198–1206. 10.1111/liv.12370. [PubMed: 24164865]
- Backus LI, Boothroyd DB, Phillips BR, Belperio P, Halloran J, & Mole LA (2011). A sustained virologic response reduces risk of all-cause mortality in patients with hepatitis C. *Clinical Gastroenterology and Hepatology : the Official Clinical Practice Journal of the American Gastroenterological Association*, 9(6), 509–516. 10.1016/j.cgh.2011.03.004e501. [PubMed: 21397729]
- Bajis S, Dore GJ, Hajarizadeh B, Cunningham EB, Maher L, & Grebely J (2017). Interventions to enhance testing, linkage to care and treatment uptake for hepatitis C virus infection among people who inject drugs: A systematic review. *The International Journal of Drug Policy*, 47, 34–46. 10.1016/j.drugpo.2017.07.002. [PubMed: 28797498]

- Barua S, Greenwald R, Grebely J, Dore GJ, Swan T, & Taylor LE (2015). Restrictions for medicaid reimbursement of sofosbuvir for the treatment of hepatitis C virus infection in the United States. *Annals of Internal Medicine*, 163(3), 215–223. 10.7326/M15-0406. [PubMed: 26120969]
- Bassett IV, Wilson D, Taaffe J, & Freedberg KA (2015). Financial incentives to improve progression through the HIV treatment cascade. *Current Opinion in HIV and AIDS*, 10(6), 451–463. 10.1097/COH.0000000000000196. [PubMed: 26371461]
- Bruggmann P, & Grebely J (2015). Prevention, treatment and care of hepatitis C virus infection among people who inject drugs. *The International Journal of Drug Policy*, 26(Suppl 1), S22–26. 10.1016/j.drugpo.2014.08.014. [PubMed: 25245939]
- Centers for Disease, C., & Prevention (2010). Syringe exchange programs — United States, 2008. *MMWR Morbidity and Mortality Weekly Report*, 59(45), 1488–1491. [PubMed: 21085091]
- Chawarski MC, Pakes J, & Schottenfeld RS (1998). Assessment of HIV risk. *Journal of Addictive Diseases*, 17(4), 49–59. 10.1300/J069v17n04_05.
- Day E, Hellard M, Treloar C, Bruneau J, Martin NK, Ovrehus A, et al. (2018). Hepatitis C elimination among people who inject drugs: Challenges and recommendations for action within a health systems framework. *Liver International : Official Journal of the International Association for the Study of the Liver*, 39(1), 20–30. 10.1111/liv.13949. [PubMed: 30157316]
- Degenhardt L, Peacock A, Colledge S, Leung J, Grebely J, Vickerman P, et al. (2017). Global prevalence of injecting drug use and sociodemographic characteristics and prevalence of HIV, HBV, and HCV in people who inject drugs: a multistage systematic review. *The Lancet Global Health*, 5(12), e1192–e1207. 10.1016/S2214-109X(17)30375-3. [PubMed: 29074409]
- Des Jarlais DC, Nugent GV, & Solberg A (2014). The dave purchase memorial 2014 national survey of syringe exchange programs: Summary of results 2014. Retrieved from Tacoma, WA: North American Syringe Exchange Network https://www.nasen.org/site_media/files/bis2013/2013-survey-results-presentation-final.pptx.
- Des Jarlais DC, Nugent A, Solberg A, Feelemyer J, Mermin J, & Holtzman D (2015). Syringe service programs for persons who inject drugs in urban, suburban, and rural areas - United States, 2013. *MMWR Morbidity and Mortality Weekly Report*, 64(48), 1337–1341. 10.15585/mmwr.mm6448a3. [PubMed: 26655918]
- Dieperink E, Pocha C, Thuras P, Knott A, Colton S, & Ho SB (2014). All-cause mortality and liver-related outcomes following successful antiviral treatment for chronic hepatitis C. *Digestive Diseases and Sciences*, 59(4), 872–880. 10.1007/s10620-014-3050-5. [PubMed: 24532254]
- Dore GJ, Altice F, Litwin AH, Dalgard O, Gane EJ, Shibolet O, et al. (2016). Elbasvir-grazoprevir to treat hepatitis C virus infection in persons receiving opioid agonist therapy: A randomized trial. *Annals of Internal Medicine*, 165(9), 625–634. 10.7326/M16-0816. [PubMed: 27537841]
- Eckhardt B, Winkelstein ER, Shu MA, Carden MR, McKnight C, Des Jarlais DC, et al. (2017). Risk factors for hepatitis C seropositivity among young people who inject drugs in New York City: Implications for prevention. *PloS One*, 12(5), 10.1371/journal.pone.0177341e0177341.
- El-Sadr WM, Donnell D, Beauchamp G, Hall HI, Torian LV, Zingman B, et al. (2017). Financial incentives for linkage to care and viral suppression among HIV-Positive patients: A randomized clinical trial (HPTN 065). *JAMA Internal Medicine*, 177(8), 1083–1092. 10.1001/jamainternmed.2017.2158. [PubMed: 28628702]
- Fishbein DA, Lo Y, Reinus JF, Gourevitch MN, & Klein RS (2004). Factors associated with successful referral for clinical care of drug users with chronic hepatitis C who have or are at risk for HIV infection. *Journal of Acquired Immune Deficiency Syndromes*, 37(3), 1367–1375. [PubMed: 15483466]
- Fox AD, Chamberlain A, Frost T, & Cunningham CO (2015). Harm reduction agencies as a potential site for buprenorphine treatment. *Substance Abuse*, 0 10.1080/08897077.2015.1011820.
- Giles EL, Robalino S, McColl E, Sniehotta FF, & Adams J (2014). The effectiveness of financial incentives for health behaviour change: Systematic review and meta-analysis. *PloS One*, 9(3), 10.1371/journal.pone.0090347e90347.
- Grebely J, Bruneau J, Bruggmann P, Harris M, Hickman M, Rhodes T, et al. (2017). Elimination of hepatitis C virus infection among PWID: The beginning of a new era of interferon-free DAA

- therapy. *The International Journal of Drug Policy*, 47, 26–33. 10.1016/j.drugpo.2017.08.001. [PubMed: 28888558]
- Grebely J, Genoway K, Khara M, Duncan F, Viljoen M, Elliott D, et al. (2007). Treatment uptake and outcomes among current and former injection drug users receiving directly observed therapy within a multidisciplinary group model for the treatment of hepatitis C virus infection. *The International Journal of Drug Policy*, 18(5), 437–443. 10.1016/j.drugpo.2007.01.009. [PubMed: 17854734]
- Grebely J, Matthews GV, Lloyd AR, & Dore GJ (2013). Elimination of hepatitis C virus infection among people who inject drugs through treatment as prevention: Feasibility and future requirements. *Clinical Infectious Diseases : an Official Publication of the Infectious Diseases Society of America*, 57(7), 1014–1020. 10.1093/cid/cit377. [PubMed: 23728143]
- Grebely J, Dalgard O, Conway B, Cunningham EB, Bruggmann P, Hajarizadeh B, et al. (2018). Sofosbuvir and velpatasvir for hepatitis C virus infection in people with recent injection drug use (SIMPLIFY): an open-label, single-arm, phase 4, multicentre trial. *The Lancet Gastroenterology & Hepatology*, 3(3), 153–161. 10.1016/S2468-1253(17)30404-1. [PubMed: 29310928]
- Grebely J, Larney S, Peacock A, Colledge S, Leung J, Hickman M, et al. (2019). Global, regional, and country-level estimates of hepatitis C infection among people who have recently injected drugs. *Addiction*, 114(1), 150–166. 10.1111/add.14393. [PubMed: 30035835]
- Hajarizadeh B, Grebely J, & Dore GJ (2013). Epidemiology and natural history of HCV infection. *Nature Reviews Gastroenterology & Hepatology*, 10(9), 553–562. 10.1038/nrgastro.2013.107. [PubMed: 23817321]
- Hallinan R, Byrne A, Agho K, & Dore GJ (2007). Referral for chronic hepatitis C treatment from a drug dependency treatment setting. *Drug and Alcohol Dependence*, 88(1), 49–53. 10.1016/j.drugalcdep.2006.09.018. [PubMed: 17067763]
- Hellard M, McBryde E, Sacks Davis R, Rolls DA, Higgs P, Aitken C, et al. (2015). Hepatitis C transmission and treatment as prevention - the role of the injecting network. *The International Journal of Drug Policy*, 26(10), 958–962. 10.1016/j.drugpo.2015.05.006. [PubMed: 26072105]
- Hellard M, Sacks-Davis R, & Gold J (2009). Hepatitis C treatment for injection drug users: A review of the available evidence. *Clinical Infectious Diseases : an Official Publication of the Infectious Diseases Society of America*, 49(4), 561–573. 10.1086/600304. [PubMed: 19589081]
- Hochstatter K, Westergaard R, Hess T, Hull S, & Peng M (2016). The effects of syringe exchange program access on hepatitis C screening among people who inject drugs. *Open Forum Infectious Diseases*, 1(Suppl 1) 2016.
- Hochstatter KR, Hull SJ, Stockman LJ, Stephens LK, Olson-Streed HK, Ehlenbach WJ, et al. (2017). Using database linkages to monitor the continuum of care for hepatitis C virus among syringe exchange clients: Experience from a pilot intervention. *The International Journal of Drug Policy*, 42, 22–25. 10.1016/j.drugpo.2016.12.006. [PubMed: 28126684]
- Information Mediary Corp Information mediary corp. Retrieved from <http://www.informationmediary.com/med-ic>.
- Iversen J, Grebely J, Catlett B, Cunningham P, Dore GJ, & Maher L (2017). Estimating the cascade of hepatitis C testing, care and treatment among people who inject drugs in Australia. *The International Journal of Drug Policy*, 47, 77–85. 10.1016/j.drugpo.2017.05.022. [PubMed: 28578863]
- Joseph R, Kofman A, Larney S, & Fitzgerald P (2014). Hepatitis C prevention and needle exchange programs in Rhode island: ENCORE. *R I Med J*, 97(7), 31–34 2013.
- Lagarde M, Haines A, & Palmer N (2007). Conditional cash transfers for improving uptake of health interventions in low- and middle-income countries: A systematic review. *JAMA*, 298(16), 1900–1910. 10.1001/jama.298.16.1900. [PubMed: 17954541]
- Martin NK, Thornton A, Hickman M, Sabin C, Nelson M, Cooke GS, et al. (2016). Can hepatitis C virus (HCV) direct-acting antiviral treatment as prevention reverse the HCV epidemic among men who have sex with men in the United Kingdom? Epidemiological and modeling insights. *Clinical Infectious Diseases : an Official Publication of the Infectious Diseases Society of America*, 62(9), 1072–1080. 10.1093/cid/ciw075. [PubMed: 26908813]

- Martin NK, Vickerman P, Grebely J, Hellard M, Hutchinson SJ, Lima VD, et al. (2013). Hepatitis C virus treatment for prevention among people who inject drugs: Modeling treatment scale-up in the age of direct-acting antivirals. *Hepatology*, 58(5), 1598–1609. 10.1002/hep.26431. [PubMed: 23553643]
- McLellan AT, Kushner H, Metzger D, Peters R, Smith I, Grissom G, et al. (1992). The fifth edition of the addiction severity index. *Journal of Substance Abuse Treatment*, 9(3), 199–213. [PubMed: 1334156]
- Mehta SH, Genberg BL, Astemborski J, Kavasery R, Kirk GD, Vlahov D, et al. (2008). Limited uptake of hepatitis C treatment among injection drug users. *Journal of Community Health*, 33(3), 126–133. 10.1007/s10900-007-9083-3. [PubMed: 18165889]
- Metsch LR, Feaster DJ, Gooden L, Matheson T, Stitzer M, Das M, et al. (2016). Effect of patient navigation with or without financial incentives on viral suppression among hospitalized patients with HIV infection and substance use: A randomized clinical trial. *JAMA*, 316(2), 156–170. 10.1001/jama.2016.8914. [PubMed: 27404184]
- Midgard H, Bramness JG, Skurtveit S, Haukeland JW, & Dalgard O (2016). Hepatitis C Treatment Uptake among Patients Who Have Received Opioid Substitution Treatment: A Population-Based Study. *PloS One*, 11(11), 10.1371/journal.pone.0166451e0166451.
- Norton BL, Fleming J, Bachhuber MA, Steinman M, DeLuca J, Cunningham CO, et al. (2017). High HCV cure rates for people who use drugs treated with direct acting antiviral therapy at an urban primary care clinic. *The International Journal of Drug Policy*, 47, 196–201. 10.1016/j.drugpo.2017.07.021. [PubMed: 28811158]
- NYC Department of Health and Mental Hygiene (2017). Hepatitis B and C annual report
- Operario D, Kuo C, Sosa-Rubi SG, & Galaraga O (2013). Conditional economic incentives for reducing HIV risk behaviors: Integration of psychology and behavioral economics. *Health Psychology : Official Journal of the Division of Health Psychology, American Psychological Association*, 32(9), 932–940. 10.1037/a0032760.
- Recommendations for testing, managing, and treating hepatitis C (2017). Infectious diseases society of America/American association for the study of the liver Retrieved from <http://www.hcvguidelines.org>.
- Rigsby MO, Rosen MI, Beauvais JE, Cramer JA, Rainey PM, O'Malley SS, et al. (2000). Cue-dose training with monetary reinforcement: Pilot study of an antiretroviral adherence intervention. *Journal of General Internal Medicine*, 15(12), 841–847. [PubMed: 11119180]
- Rosen MI, Dieckhaus K, McMahon TJ, Valdes B, Petry NM, Cramer J, et al. (2007). Improved adherence with contingency management. *AIDS Patient Care and STDs*, 21(1), 30–40. 10.1089/apc.2006.0028. [PubMed: 17263651]
- Salek TP, Katz AR, Lenze SM, Lusk HM, Li D, & Des Jarlais DC (2017). Seroprevalence of HCV and HIV infection among clients of the nation's longest-standing statewide syringe exchange program: A cross-sectional study of Community Health Outreach Work to prevent AIDS (CHOW). *The International Journal of Drug Policy*, 48, 34–43. 10.1016/j.drugpo.2017.06.009. [PubMed: 28779632]
- Saunders JB, Aasland OG, Babor TF, de la Fuente JR, & Grant M (1993). Development of the Alcohol Use Disorders Identification Test (AUDIT): WHO Collaborative Project on Early Detection of Persons with Harmful Alcohol Consumption–II. *Addiction*, 88(6), 791–804. [PubMed: 8329970]
- Solomon SS, Srikrishnan AK, Vasudevan CK, Anand S, Kumar MS, Balakrishnan P, et al. (2014). Voucher incentives improve linkage to and retention in care among HIV-infected drug users in Chennai, India. *Clinical Infectious Diseases : an Official Publication of the Infectious Diseases Society of America*, 59(4), 589–595. 10.1093/cid/ciu324. [PubMed: 24803381]
- Sorensen JL, Haug NA, Delucchi KL, Gruber V, Kletter E, Batki SL, et al. (2007). Voucher reinforcement improves medication adherence in HIV-positive methadone patients: A randomized trial. *Drug and Alcohol Dependence*, 88(1), 54–63. 10.1016/j.drugalcdep.2006.09.019. [PubMed: 17056206]
- Stanaway JD, Flaxman AD, Naghavi M, Fitzmaurice C, Vos T, Abubakar I, et al. (2016). The global burden of viral hepatitis from 1990 to 2013: Findings from the Global Burden of Disease Study 2013. *Lancet*, 388(10049), 1081–1088. 10.1016/S0140-6736(16)30579-7. [PubMed: 27394647]

- Sulkowski M, Ward K, Falade-Nwulia O, et al. (2017). Randomized controlled trial of cash incentives or peer mentors to improve HCV linkage and treatment among HIV/HCV coinfecting persons who inject drugs: The CHAMPS study Paper presented at the EASL, Amsterdam, Netherlands.
- Treloar C, Hull P, Dore GJ, & Grebely J (2012). Knowledge and barriers associated with assessment and treatment for hepatitis C virus infection among people who inject drugs. *Drug and Alcohol Review*, 31(7), 918–924. 10.1111/j.1465-3362.2012.00468.x. [PubMed: 22612899]
- Treloar C, Newland J, Rance J, & Hopwood M (2010). Uptake and delivery of hepatitis C treatment in opiate substitution treatment: Perceptions of clients and health professionals. *Journal of Viral Hepatitis*, 17(12), 839–844. 10.1111/j.1365-2893.2009.01250.x.s [PubMed: 20070504]
- van der Meer AJ, Veldt BJ, Feld JJ, Wedemeyer H, Dufour JF, Lammert F, et al. (2012). Association between sustained virological response and all-cause mortality among patients with chronic hepatitis C and advanced hepatic fibrosis. *JAMA*, 308(24), 2584–2593. 10.1001/jama.2012.144878. [PubMed: 23268517]

Keypoints

Persons who inject drugs (PWID) are not being linked to life-saving HCV treatment. In this study, contingency management improved HCV linkage to care for persons accessing a syringe exchange program. Contingency management may improve the HCV cascade of care for PWID.

Fig. 1. Flowchart of participants in a trial of contingency management versus an enhanced standard of care to increase linkage to HCV care among syringe exchange program clients.

Fig. 2. Cascade of HCV care among participants in a trial of a contingency management versus an enhanced standard of care to increase linkage to HCV care among syringe exchange program clients (n = 39).

Fig. 3.

Weekly medication adherence among participants in a trial of a contingency management versus an enhanced standard of care to increase linkage to HCV care among syringe exchange program clients ($n = 13$)^{**} Mean daily adherence was 81% at week one and decreased over the 12-week treatment period (-1.4 percentage points per week, 95% CI: $-2.4, -0.3$, $p = 0.01$).

Table 1

Study elements and clinical care after enrollment from the NSP.

Time (weeks)	HCV Clinical Visit, Identical for Both Study Arms ^a	Medication Delivery by the Clinician, Identical for Both Study Arms	Research Visit for All Participants, Identical for Both Study Arms	Reimbursement for Participants by Study Staff, CM Arm only (Total possible reimbursement: \$345)
0	Baseline evaluation (linkage to care)	–	Questionnaire Given	\$25
2	Review of lab results	–		\$25
4	HCV treatment initiation	2 weeks of blister packs		\$25
6	HCV treatment week 2	2 weeks of blister packs		\$25 + \$10 for each blister pack returned
8	HCV treatment week 4	4 weeks of blister packs		\$25 + \$10 for each blister pack returned
12	HCV treatment week 8	4 weeks of blister packs		\$25 + \$10 for each blister pack returned
16	HCV treatment ^b week 12	–		\$25 + \$10 for each blister pack returned
20	SVR4	–		\$25
24	SVR12	–		\$25

^aClinical visits were per clinic protocol; week 2, week 8, and SVR4 visits were primarily for adherence checks, medication delivery, and clinical engagement.^bAll participants were genotype 1 and received sofosbuvir/ledipasvir therapy for 12 weeks.

Table 2

Demographic and clinical characteristics of all enrolled participants in a trial of a contingency management versus an enhanced standard of care to increase linkage to HCV care among needle and syringe program clients(n = 39).

Characteristic	Contingency management (n = 19) n (%)	Enhanced standard of care (n = 20) n (%)	P-value
Age, mean (SD)	47 (4055)	46 (3554)	0.41
Male sex	14 (74)	12 (60)	0.37
Race/ethnicity			
Black, non-Hispanic	5 (26)	3 (15)	0.30
Hispanic, of any race	11 (58)	16 (80)	
Whitec White	3 (16)	1 (5)	

Table 3

Demographic and clinical characteristics of participants linked to care and treatment eligible in a trial of a contingency management versus an enhanced standard of care to increase linkage to HCV care among needle and syringe program clients(n = 16).

Characteristics	Contingency management (n = 12)	Enhanced standard of care (n = 4)	P-value
Age, mean (SD)	47.9 (8)	53.3 (5)	0.87
Male sex	9 (75)	2 (50)	0.35
Race/ethnicity			
Black, non-Hispanic	5 (42)	2 (50)	0.83
Hispanic, of any race	5 (42)	1 (25)	
White	2 (17)	1 (25)	
Housing			
Homeless	6 (50)	2 (50)	0.92
Single Room Occupancy (SRO)	2 (17)	1 (25)	
Rents Apartment	4 (33)	1 (25)	
Self-Reported Substance Use			
Alcohol	2 (17)	2 (50)	0.18
Heroin	6 (50)	2 (50)	1.0
Other Opioids	0 (0)	1 (25)	0.07
Cocaine	2 (17)	2 (50)	0.18
Cannabis	4 (33)	2 (50)	0.55
Self-Reported Injection Drug Use	5 (42)	2 (50)	0.77
HIV Positive	1 (25)	3 (75)	0.01
Genotype			
1a	11 (92)	1 (33)	0.38
1b	1 (8)	2 (67)	
Fibrosure (n = 12)			
F0/F1/F2	4 (44)	1 (33)	0.74
F3/F4	5 (56)	2 (67)	
HCV Treatment Regimen			
Sofosbuvir/Ledipasvir	9 (100)	4 (100)	1.0